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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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10/672,280

09/26/2003

Gregory Alan Lazar

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11/16/2006

DORSEY & WHITNEY LLP
555 CALIFORNIA STREET, SUITE 1000
SUITE 1000
SAN FRANCISCO, CA 94104

EXAMINER

CROWDER, CHUN

ART UNIT

PAPER NUMBER

1644

DATE MAILED: 11/16/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

10/672,280

Applicant(s)

LAZAR ET AL.

Examiner

Chun Crowder

Art Unit

1644

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 07 September 2006.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-3,5-38,40-51,53-55,57-59,61-63,65 and 67-87 is/are pending in the application.
- 4a) Of the above claim(s) See Continuation Sheet is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-3, 6, 7, 10-14, 16, 18, 19, 21-28, 34, 40, 41, 59, 63, 79, 80, 86, and 87 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|---|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413)
Paper No(s)/Mail Date: _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08)
Paper No(s)/Mail Date: _____ | 6) <input type="checkbox"/> Other: _____ |

Continuation of Disposition of Claims: Claims withdrawn from consideration are 5, 8,9,15,17,20,29-33,35-38,42-51,53-55,57,58,61,62,67-78 and 81-85.

DETAILED ACTION

1. Applicant's amendments, filed 09/07/2006, are acknowledged.

Claims 4, 39, 52, 56, 60, 64, and 66 have been canceled.

Claims 1-3, 5-9, 12-14, 18, 26, 32-34, 40, 41, 45, 47, 55, 57, 61-63, 65, 67-69, 82, and 85 have been amended.

Claims 86 and 87 have been added.

Claims 1-3, 5-38, 40-51, 53-55, 57-59, 61-63, 65, 67-87 are pending.

Applicant asserts that claims 16, 28, 30-31, 41, 47-51, 53, 79, and 80 are directed to the elected species; therefore, the claims should not be withdrawn.

It is noted that the originally elected species are an antibody, IgG1, targeting CD20, 239D substitution, increased affinity for FcγR and no carbohydrate modification. Thus, claims 30-31 are not under consideration because they are drawn to reduced affinity for FcγR.

Further, claims 47-51 are drawn to an aglycosylated Fc variant that is modified to remove carbohydrate; therefore, claims 47-51 are drawn to nonelected species. Furthermore, claim 53 is dependent on canceled claim 52 that was dependent on claim 47, thus for examination purposes, claim 53 is read as dependent on claim 47 and is drawn to nonelected species. Moreover, applicant has canceled the elected species of "239D" in claim 15.

Consequently, claims 15, 30-31, 47-51 and 53 have been withdrawn because they are drawn to nonelected species.

In addition, applicant has indicated on page 14 of the Remarks that claim 3 had been canceled. However, the status of claim 3 is "currently amended", not canceled. For examination purposes, claim 3 is read as dependent on claim 2 as indicated in the listing of claims. Applicant is requested to clarify the status of claim 3.

Claims 5, 8, 9, 15, 17, 20, 29-33, 35-38, 42-51, 53-55, 57, 58, 61, 62, 67-78, and 81-85 have been withdrawn from further consideration under 37 C.F.R. 1.142(b) as being drawn to nonelected inventions.

Claims 1-3, 6, 7, 10-14, 16, 18, 19, 21-28, 34, 40, 41, 59, 63, 79, 80, 86, and 87 are under consideration in the instant application as they ready on the originally elected invention of Group I and species an antibody, IgG1, targeting CD20, 239D substitution, increased affinity for FcγR and no carbohydrate modification.

2. This Office Action will be in response to applicant's arguments, filed 09/07/2006.

The rejections of record can be found in the previous Office Action, mailed 07/26/2006.

The text of those Sections of Title 35 U.S.C. not included in this Action can be found in a prior Action.

3. Applicant's arguments regarding priority issues are acknowledged. Applicant has not provided support for the claimed limitations of "position....239" of the Fc region in the provisional application USSNs 60/414,433 and 60/442,301; thus the instant claims are not accorded the priority date of 09/27/2002 and 01/23/2003.

4. Claims 16 and 41 are objected to because claim 16 is dependent on nonelected claim 15; claim 41 is dependent on canceled claim 39. Appropriate correction is required.

For examination purposes, claim 16 is read as dependent on claim 14 and claim 41 as dependent on claim 34.

5. Claims 6, 79, and 80 are rejected under **35 U.S.C. 112, second paragraph**, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention for reasons of record.

A) Claim 6 is indefinite in the recitation of “substantially human” because the metes and bounds of the claims is unclear and ambiguous.

Applicant asserts that the term “substantially” has been deleted. However, claim 6 still recites the term, therefore remains indefinite.

B) Claim s 79 and 80 recites the limitation "antibody". There is insufficient antecedent basis for this limitation in the claim.

C) Applicant is reminded that any amendment must point to a basis in the specification so as not to add new matter. See MPEP 714.02 and 2163.06.

6. Claims 1-3, 6, 7, 10-14, 16, 18, 19, 21-28, 34, 40, 41, 59, 79, and 80 are rejected under **35 U.S.C. 112, first paragraph**, as failing to comply with the enablement requirement. The claims contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention for reasons of record.

Claims 1-3, 6, 7, 10-14, 16, 18, 19, 21-28, 34, 40, 41, 59, 79, and 80 recite “a polypeptide comprising an Fc variant” as part of the invention.

Applicant’s arguments have been fully considered but have not been found convincing.

Applicant argues that the claims have been amended to recite specific substitution positions within the Fc variant; the newly added claims 86 and 87 now recite “antibody” and “Fc fusion”. Further, applicant argues that the instant specification has defined the “Fc fusion” as a protein wherein one or more polypeptides are operably linked to Fc; thus, Fc fusion is meant to be synonymous with “immunoadhesin”, “Ig fusion”, “Ig chimera” and “receptor globulin”.

This is not found persuasive for following reasons:

Contrary to applicant's assertion, the specification teaches that a "a polypeptide comprising an Fc variant" according to the definition of a variant polypeptide meant an Fc sequence that differs from a parent Fc sequence by at least one amino acid modification, e.g. from about one to about ten amino acid modification, or possess at least 80% homology with a parent polypeptide sequence.

Amending the claims to recite the specific amino acid substitution positions does not change the scope of claims, which are drawn to an extensive "a polypeptide comprising an Fc variant". There does not appear to be sufficient guidance in the specification as filed as to how the skilled artisan would make and use the claimed "a polypeptide comprising an Fc variant". The specification provides insufficient direction or guidance regarding how to make and use "a polypeptide comprising an Fc variant" as broadly defined by the claims.

Therefore, The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

Applicant is once again suggested to amend the claimed Fc variant/polypeptide to antibody and/or Immunoadhesin as disclosed on pages 22-26 of the instant specification to obviate this rejection.

The rejections of record are maintained for the reasons of record, as they apply to the amended claims. The rejections of record are incorporated by reference herein as if reiterated in full.

7. Claims 1-3, 6, 7, 10-14, 16, 18, 19, 21-28, 34, 40, 41, 59, 79, and 80 are rejected under **35 U.S.C. 112, first paragraph**, as failing to comply with the written description requirement. The claims contain subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The following *written description* rejection is set forth herein.

Applicant's arguments and the examiner's rebuttal are essentially the same as discussed above in Section 6.

Applicant is once again suggested to amend the claimed Fc variant/polypeptide to antibody and/or Immunoadhesin as disclosed on pages 22-26 of the instant specification to obviate this rejection.

8. Claims 1-3, 6, 7, 10-14, 16, 18, 19, 21-28, 34, 40, 41, 59, 63, 79, 80, 86, and 87 are rejected under **35 U.S.C. 102(b)** as being anticipated by Presta (WO 00/42072. Reference B1 on IDS) for reasons of record.

Applicant's arguments have been fully considered but have not been found convincing.

Applicant argues that Presta does not anticipate the claims because Presta does not specifically describe the claimed species of 239D; therefore Presta does not inherently teach the claimed functional limitations. Further, Presta teaches working examples of 239A that has reduced binding affinity to both FcγRIIIa and FcγRII.

This is not found persuasive for following reasons:

Contrary to applicant's assertion, Presta teaches and claims a polypeptide (e.g. antibody or immunoadhesin) comprising a variant Fc region with higher binding affinity to FcγR including FcγRIII and an amino acid substitution at positions such as 239 for improved effector functions (see entire document, particularly Summary of the Invention on pages 5-8).

Further, Presta defines "amino acid substitution" as the replacement of existing amino acid residue in a predetermined amino acid sequence with another different amino acid residue including aspartic acid (D) (e.g. see pages 14-15).

In contrast to applicant's assertions based upon the working examples of Presta, it is noted that a prior art reference must be considered in its entirety.

In contrast to appellant's assertions that Presta does not teach specific amino acid substitution at position 239 with residue aspartic acid (D), Presta clearly teaches that position 239 of the Fc region of the parent polypeptide can be substituted with any other amino acid residues including aspartic acid (D) other than the parent residue serine (S) (e.g. see pages 14-15).

Even if Presta discloses a genus of natural and non-natural amino acids, Presta clearly teaches the species of the amino acid residue aspartic acid (D) as claimed.

It is noted that when the species is clearly named, the species claim is anticipated no matter how many other species are additionally named. Ex parte A, 17 USPQ2d 1716 (Bd. Pat. App. & Inter. 1990). Also see MPEP 2131.02.

In conclusion, the comprehensiveness of the explicit listing of the known naturally occurring amino acids and disclosed non-naturally occurring amino acids in Presta does not negate the fact that the amino acid substitution by aspartic acid (D) in position 239 of the Fc region as claimed was specifically taught.

Given the reference antibody variant comprises amino acid substitution at the same position (239) with the same residue aspartic acid (D) as the claimed polypeptide variant comprising an Fc variant, the claimed functional limitations associated with the polypeptide variant would be inherent properties of the reference polypeptide.

In addition, applicant asserts that the Examiner cited In re Sivaramakrishnan (see page 19 of the Remark). It is not clear when and where In re Sivaramakrishnan was cited by the Examiner.

Therefore, the teachings of Presta anticipate the claimed invention.

The rejections of record are maintained for the reasons of record, as they apply to the amended and newly added claims. The rejections of record are incorporated by reference herein as if reiterated in full.

9. Claims 1-3, 6, 7, 10-14, 16, 18, 19, 21-28, 34, 40, 41, 59, 63, 79, 80, 86, and 87 are rejected under 35 U.S.C. 102(e) as being anticipated by Presta (US Patent 6,737,056. Reference A97 on IDS) for reasons of record.

Applicant's arguments and the examiner's rebuttal are essentially the same as discussed above in Section 8.

Therefore, the reference teachings anticipate the claimed invention.

10. Given the absence of additional rebuttal in applicant's amendment to the outstanding nonstatutory obviousness-type double patenting rejections of record over USSNs: 11/483,378, 11/483,250, 10/822,231, 11/124,620, and 11/396,495, the rejections are maintained for reasons of record.

11. Upon further consideration as well as applicant's amendments, the previous rejections under 35 U.S.C. 112, second paragraph regarding "modulate", "effector function", and "FcγRIIIa-fold: FcγRIIb-fold ratio" have been withdrawn.

Upon further consideration as well as applicant's amendments, the previous rejection under 35 U.S.C. 112, second paragraph regarding "substantially human" and/or "substantially mouse, substantially rat or substantially monkey" against claims 12, 13, 18, and 43 has been withdrawn.

12. Conclusion: No claim is allowed.

13. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Chun Crowder whose telephone number is (571) 272-8142. The examiner can normally be reached Monday through Friday from 8:30 am to 5:00 pm. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached on (571) 272-0841. The fax number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Chun Crowder, Ph.D.

Patent Examiner

November 3, 2006

Phillip Cambel
PHILLIP CAMBEL, PH.D.
PRIMARY EXAMINER
TZ 1600
11/5/06